I. COMPARISON OF INTERFERENCE VALUES OF METHOXYL AND HYDROXYL GROUPS IN RESOLVABLE BIPHENYLS

II. SYNTHESIS OF DESAPOGOSSYPOLONE TETRAMETHYL ETHER

BY

HOWARD MAPLE TEETER

B.S., Bradley Polytechnic Institute, 1937

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AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY IN THE GRADUATE SCHOOL OF THE UNIVERSITY OF ILLINOIS,

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I. COMPARISON OF INTERFERENCE VALUES OF METHOXYL AND HYDROXYL GROUPS IN RESOLVABLE BIPHENYLS

Many investigations have been made relative to the comparative effects of various *ortho* substituents on the restricted rotation of biphenyl derivatives. Of these investigations, the study of the steric effect of the group attached to the atom combined with the ring has been of particular interest because of the insight gained into the structure of the entire grouping attached to the ring.

The simplest case would be the comparison of the steric effects of methoxyl and hydroxyl groups. A study [1] of 2-nitro-6-carboxy-2′-alkoxybiphenyl showed that the steric effect of the alkoxyl groups increased in the order CH_3O, C_2H_5O, n-C_3H_7O. This result, combined with calculations based upon Pauling's tables [2] of atomic radii and Sutton and Brockway's [2] evaluation of the oxygen bond angle in ethers, indicated that hydroxyl should be the smaller group. Other experimental data [3] of an indirect nature seem to show that the two groups are equivalent. A comparison of the optical stability of 2-methyl-4-carboxy-6-nitro-2′-methoxybiphenyl and the corresponding hydroxyl derivative was therefore undertaken.

EXPERIMENTAL

Methyl 3-methyl-4-bromo-5-nitrobenzoate was prepared from *m*-toluidine by the following steps: acetylation, bromination, deacetylation, diazotization, introduction of a cyano group, nitration, hydrolysis, and esterification. The structure of the resulting ester was proved by conversion of the intermediate 3-methyl-4-bromo-5-nitrobenzonitrile to the corresponding phenol by fusion with sodium acetate and acetamide. Hydrolysis and esterification gave a known compound, methyl 3-methyl-4-hydroxy-5-nitrobenzoate.

Condensation of methyl 3-methyl-4-bromo-5-nitrobenzoate with *o*-iodoanisole by means of copper bronze at 270° gave 2-methyl-4-carboxy-6-nitro-2′-methoxybiphenyl in 20 per cent yield. It could be demethylated in good yield by the action of hydrobromic acid in glacial acetic acid solution.

The brucine salt of the methoxy compound was prepared. Only one salt was obtained; it did not mutarotate. By decomposition, the methoxy acid was obtained in an optically active form, specific rotation —7.9°. At 35° in glacial acetic acid solution, the acid

racemized with a half life of 207 minutes. In boiling glacial acetic acid, the half life was 11 minutes. On the other hand, the hydroxy acid could not be resolved by means of either brucine or strychnine. Careful fractionation gave only one salt in each case, and decomposition of the various fractions gave an inactive acid.

SUMMARY

2-Methyl-4-carboxy-6-nitro-2′-methoxybiphenyl and 2-methyl 4-carboxy-6-nitro-2′-hydroxybiphenyl have been prepared. The methoxy acid was obtained in an active form which had a half life of 207 minutes at 35°. The hydroxy acid could not be resolved. On the basis of this evidence, it is concluded that the hydroxyl group is smaller than the methoxyl group.

II. SYNTHESIS OF DESAPOGOSSYPOLONE TETRAMETHYL ETHER

INTRODUCTION

Adams [4] assigned to gossypol, the yellow coloring matter of cottonseed, the formula 2,2-bi-1,6,7-trihydroxy-3-methyl-5-isopropyl-8-aldehydonaphthalene. However, no degradation product has been proved to contain the binaphthyl nucleus. The purpose of this research was first to investigate suitable methods of preparation of binaphthyl derivatives and second to synthesize desapogossypolone tetramethyl ether.

EXPERIMENTAL

Two general methods are available for the synthesis of desapogossypolone tetramethyl ether; namely, formation of a binaphthyl by union of appropriately substituted naphthalene derivatives and construction of a binaphthyl upon a biphenyl derivative as foundation.

Four variations of the first method were studied: Pummerer's quinone reaction,[5] the Ullmann reaction, the ferric chloride oxidation,[6] and the coupling of diazotized amines. Pummerer's quinone reaction was applied to 2-methyl-1,4-naphthoquinone. The Ullmann reaction was attempted with both the diacetate and the dimethyl ether of 2-methyl-3-bromo-1,4-naphthohydroquinone, for which compounds successful methods of synthesis were developed. The ferric chloride oxidation was carried out upon 2-methyl-1,4-naphthohydroquinone. All of these reactions failed, presum-

ably because of the blocking effect of the 2 methyl group. The amine coupling was carried out upon 1-nitro-2-aminonaphthalene using a basic cuprous oxide catalyst.[7] An 11 per cent yield of 1,1′-dinitro-2,2′-binaphthyl was obtained.

It was proposed, in connection with the second general method of synthesis of binaphthyls, to add dimethoxybutadiene to 2,2-bi-3-methylbenzoquinone followed by dehydrogenation to the binaphthyl. Two phases were studied: the synthesis of the bitolyldiquinone and the addition of butadiene to toluquinone. 2,2′,5,5′-Tetra-amino-6,6′-dimethylbiphenyl was prepared from 2,2′-dinitro-6,6′-dimethylbiphenyl by successive reduction, acetylation, nitration, deacetylation, and reduction. This tetra-amine, however, could not be oxidized by manganese dioxide or potassium dichromate to the desired diquinone.

Addition of butadiene to toluquinone followed by isomerization gave 5,8-dihydro-2-methyl-1,4-naphthohydroquinone.[8] The diacetate was dehydrogenated with chloranil [9] to give a 30 per cent yield of 2-methyl-1,4-naphthohydroquinone diacetate.

SUMMARY

Pummerer's quinone reaction, the Ullmann reaction, and the ferric chloride oxidation failed when applied to derivatives of 2-methyl-1,4-naphthoquinone. The coupling of diazotized amines was applied to 1-nitro-2-aminonaphthalene. An 11 per cent yield of the binaphthyl was obtained. An attempted synthesis of 2,2-bi-3-methylbenzoquinone was not successful. However, the addition product of butadiene and toluquinone could be dehydrogenated to a naphthalene derivative in fair yields.

REFERENCES

[1] Li and Adams, J. Am. Chem. Soc., **57**, 1565 (1935).

[2] Pauling, Proc. Natl. Acad. Sci. U. S., **20**, 336 (1934); Sutton and Brockway, J. Am. Chem. Soc., **57**, 473 (1935).

[3] Stanley and Adams, J. Am. Chem. Soc., **52**, 1200 (1930); Shildneck and Adams, *ibid.*, **53**, 343, 2203 (1931).

[4] Adams, Morris, Geissman, Butterbaugh, and Kirkpatrick, *ibid.*, **60**, 2193 (1938).

[5] Pummerer, Ber., **70**, 2281 (1937); **72**, 1627 (1939).

[6] Walder, *ibid.*, **15**, 2166 (1882).

[7] Herz and Zerweck, Ger. Patent, 445, 390.

[8] Chuang and Han, Ber., **68**, 876 (1935).

[9] Arnold, J. Am. Chem. Soc., **61**, 1407 (1939); **62**, 983 (1940).

VITA

The author was born at Peoria, Illinois, on October 14, 1915. He attended the public schools of that city. He then entered Bradley Polytechnic Institute, receiving the degree of Bachelor of Science in 1937. He continued his work in the Graduate School of the University of Illinois. In 1938 the degree of Master of Science was awarded him. During his residence at the University, he held the following appointments: Scholar in Chemistry, 1937-1938; Fellow in Chemistry, 1938-1940. He is a member of Phi Lambda Upsilon, Phi Kappa Phi, Sigma Xi, and the American Chemical Society.

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